epothilones, halicondrins, benomyl and mebendazole directly inhibit cell division by binding to tubulin which subsequently arrests cells in mitosis. This is the basis of their therapeutic value, such as treating gout with colchicine, restenosis with paclitaxel, cancer with paclitaxel, vinblastine, epothilones and halichondrins, and fungal infections with benomyl and malaria and helminths with mebendazole. We have developed two compounds which set two new precedents for tubulin ligands: First, they covalently bind to tubulin creating a stable conjugate that inhibits tubulin polymerization. And second: they arrest cells in the S-phase of the cell cycle. We have shown that there is therapeutic potential for these ligands and their novel characteristics such as low resistant cell line generation rates and short exposure time make them ideal for therapeutic regimes where side effects of chemotherapy are a major issue. " "

The original first paragraph read:

" " **I. <u>Field of the Invention</u>**

Tubulin is an intra-cellular protein that polymerizes to form structural components of the cytoskeleton called microtubules. Typical tubulin ligands such as colchicine, paclitaxel, vinblastine, epothilones, halicondrins, benomyl and mebendazole directly inhibit cell division by binding to tubulin which subsequently arrests cells in mitosis. This is the basis of their therapeutic value, such as treating gout with colchicine, restenosis with paclitaxel, cancer with paclitaxel, vinblastine, epothilones and halichondrins, and fungal infections with benomyl and malaria and helminths with mebendazole. We have developed two compounds which set two new precedents for tubulin ligands: First, they covalently bind to tubulin creating a stable conjugate that inhibits tubulin polymerization. And second: they arrest cells in the S-phase of the cell cycle. We have shown that there is therapeutic potential for these ligands and their novel characteristics such as low resistant cell line generation rates and short exposure time make them ideal for therapeutic regimes where side effects of chemotherapy are a major issue. " "

Thank you for incorporating this amendment.

Yours sincerely,

Ashley Davis.